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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/899,856	07/24/97	BLUMBERG R	[illegible]

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EXAMINER	
CUNNINGHAM, T	

ART UNIT	PAPER NUMBER
1641	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 08/899,856	Applicant(s) Blumberg et al.
	Examiner Thomas Cunningham	Group Art Unit 1644

☒ Responsive to communication(s) filed on *Apr 26, 1999*.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *18-25* is/are pending in the application.

Of the above, claim(s) *22* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *18-21 and 23-25* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *3, 8, 11*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

1. Applicant's election without traverse of (A) the FcRn binding partners "IgG Fc fragments", (B) the bioactive substances "proteins or peptides" and (C) method of delivery "oral delivery" in Paper No. 10 is acknowledged. Claims 18-21 and 23-25 have been examined to the extent that they embrace the elected subgenus of methods. Claim 22 is withdrawn from consideration because it does not read on oral administration.

2. Claims 18-21 and 23-25 are generic to a plurality of disclosed patentably distinct species comprising conjugates comprising different bioactive proteins, such as those enumerated on page 23 of the specification under the headings "Peptides and proteins" and "Hormones". Applicant is required under 35 U.S.C. 121 to elect a single ultimately disclosed species, even though this requirement is traversed.

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

3. Claims 18-21 and 23-25 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Reasons are set forth below.

A. In claims 18-19 and 25 it is unclear what the metes and bounds of the term "conjugate" are. Can a conjugate comprising an Fc fragment be an intact IgG molecule? Is the term "conjugate" limited to discrete moieties that are chemically coupled or cross-linked to each other as is suggested by pages 7-8 and described on pages 39-40 of the specification? Alternatively, does the term "conjugate" embrace hybrid or fusion proteins? Is the term "conjugate" limited to covalently-bound moieties or can it encompass noncovalently-associated ingredients? E.g. could an anti-insulin IgG molecule noncovalently-bound to insulin be a conjugate as is suggested by page 41 of the specification? As the Examiner is obligated to interpret this term broadly, for examination purposes it has been interpreted as reading on any protein or protein complex which comprises an Fc determinant and as encompassing both covalent and noncovalent conjugates.

B. In claim 20 it is unclear what the term "Fc fragment of IgG" means. Other than the Fc portion of an IgG molecule what segments of IgG are encompassed by the claim language? Does this read on any antibody product that comprises an Fc portion? Is this term limited to an Fc moiety as prepared by a procedure similar to that described in Example 7, page 39 of the specification? As the Examiner is obligated to interpret this term broadly, for examination purposes it has been interpreted as reading on any protein or protein complex which comprises an Fc determinant.

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 18-21 and 23-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fritsche et al., J. Allergy Clin. Immunol. 93:778-86 (April, 1994), Zanetti et al.; U.S. patent 5,658,762, Gosselin et al. 149:3477-81 (1992), Landolfi US 5,349,053 Issued Sept. 20, 1994, filed June 1, 1990), Zaghouani et al (Science 259:224, 1993) or Nemazee et al., U.S. patent 5,698,679 (12/16/97), in view Czerkinsky et al., Infect. Immun. 57:1072-7 (1989) , Simister, Fc receptors and the action of antibodies, pages 57-73 (1990) or Kim et al., Eur. J. Immunol. 24:2429 (1994).

Fritsche et al., Zanetti et al. and Gosselin et al. teach antigen-antibody (IgG) conjugates that comprise an Fc fragment and which are capable of binding to FcRn. Nemazee et al. disclose pharmaceutical preparations comprising an antigen covalently-coupled to an immunoglobulin that comprises an Fc fragment. Nemazee et al. disclose that the peptide is conjugated to the immunoglobulin component by chemical cross-linking or peptide bonding via recombinant DNA technology (see column 6, lines 47-55, in particular). Nemazee, col. 22 suggests oral administration of the conjugate. Landolfi et al disclose antigen - IgG conjugates. Landolfi et al. disclose immunoglobulin-ligand conjugates comprising a constant region (Fc portion) of IgG (see column 2, lines 40-67, in particular). Zaghouani et al. teach antigen-immunoglobulin conjugates in which the antigen is a peptide epitope derived from a pathogen (hemagglutin peptide of influenza virus) and the immunoglobulin component is IgG (that comprises an Fc fragment), see page 225, first column, in particular.. Zaghouani et al. further teach that antigen-immunoglobulin conjugates can be used as safe vaccines endowed with greater immunogenicity since immunization with influenza peptide-immunoglobulin conjugate was more efficient in eliciting an immune response than the unconjugated influenza peptide alone. Zaghouani et al. further teach that antigen-immunoglobulin conjugates have several advantages as vaccines since they exhibit a longer half-life and can be internalized into APC by means of FcR and that self molecules that

carry foreign T helper epitopes alone or in combination with a foreign B cell epitope could represent a new type of safe vaccine aimed at stimulating strong specific immunity.

To the extent that the primary references do not teach all the aspects of the instant methods, such as either oral administration of these conjugates or conjugates requiring an Fc segments for delivery of the conjugated antigen the secondary references do.

Czerkinsky et al. page 1072 teach that antigens administered orally (to a mucosal epithelial surface) result in absorption and processing by specialized cells (col. 1) and induce immune responses, especially mucosal or secretory immune responses. Simister teach that FcRn is a receptor that permits uptake of IgG from epithelial surfaces. Kim et al. teach that the FcRn receptors are localized to endosomal vesicles of the apical and basolateral cytoplasma (see page 2434, in particular). Kim et al. also disclose that radio labeled IgG1 and Fc fragments of IgG1 are transferred from the intestine into the circulation in neonatal mice fed radio labeled IgG1 or Fc fragments, see page 2431. Kim et al. teach that neonatal mice are mammals which express the FcRn receptor (see pages 2429 and 2431, in particular).

It would have been prima facie obvious to one of ordinary skill in the art at the time of invention to orally administer the antigen-antibody conjugate comprising an Fc segment of Fritsche et al., Zanetti et al., Gosselin et al. or Nemazee et al. in view of the teachings of the secondary references which indicate that oral administration of an antigen results in specific antigen uptake and induction immune responses, such as secretory or mucosal immunity.

7. Claim 18-21 and 23-25 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-20 of copending Application No. 08/374,159 in view of Zaghouani et al. (Science 259:224, 1993) or Nemazee et al. US 5,698,679 (Issued Dec. 16, 1997, filed Sep. 19, 1994). Although the conflicting claims are not identical, they are not patentably distinct from each other because 08/374,159 are drawn to method of activating or suppressing the immune response by administrating conjugate of an antigen and FcRn binding partner and compositions comprising a conjugate of an antigen and FcRn binding partner wherein the antigen characteristic of a pathogen, autoimmune disease or allergen. The claims of the instant application are drawn to method of activating or suppressing the immune response by administrating conjugate of an antigen and FcRn binding partner and compositions comprising a conjugate of an antigen and FcRn binding partner wherein the antigen characteristic of a tumor, pathogen, autoimmune disease or allergen. The methods claimed in claims 18-25 of the instant application encompass the methods of 08/374,159. One with ordinary skill in the art at the time of the invention would have been motivated to make a conjugate of an antigen and a FcRn binding partner such as IgG or Fc fragment of IgG wherein in the antigen is characteristic of a tumor (IE a tumor specific antigen) since Zaghouani et al. or Nemazee et al. teach that such an conjugate could be used to induce anti-tumor cell immune responses.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ormum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Thomas M. Cunningham, Ph.D., J.D., whose telephone number is (703) 308-3968. Dr. Cunningham can generally be reached Monday through Thursday from 7:30AM to 6:00 PM. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

TC

THOMAS M. CUNNINGHAM
PRIMARY EXAMINER
GROUP 1800